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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,803	08/24/2001	Henry Yue	PF-0695-2 CON	3863

22428 7590 08/18/2004

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,803	YUE ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,10,12-16,18,21,24,26,27,50 and 51* is/are pending in the application.

4a) Of the above claim(s) *1,2,9,12-16,18,21,24,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *3-7, 10, 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/24/01
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on April 6, 2004 has been entered.

2. Claims 8, 11, 17, 19-20, 22-23, 25, 28-49, and 52 are cancelled. Claims 1-2, 9, 12-16, 18, 21, 24, 26-27 and 50 are withdrawn as being drawn to non-elected claims. Claims 1, 3-4, 10, 51 are amended. Claims 3-7, 10, 51 are currently under consideration.

Priority

3. This application is a continuation of US application number 09/311,894 filed on May 14, 1999 which is abandoned.

Response to Arguments

4. Applicants' response to office action, amendment and arguments are fully considered and found persuasive in part.

5. With reference to the restriction requirement, Applicants' arguments regarding rejoinder of claims 9, 12-14, 26-27 drawn to method of making and method of use, are fully considered and rejoinder of claims 9, 12-14, 26-27 will be considered, upon allowance of claims 4 and 10.

6. With reference to the rejections made in the previous office action under 35 USC 112 second paragraph, Applicants arguments and amendment are fully considered and the rejections are withdrawn herein in view of the amendment.

7. With reference to the rejection made in the previous office action under 35 USC 102(b), Applicants arguments and amendment are fully considered and the rejection is withdrawn herein in view of the amendment.

8. With reference to the above rejection made in the previous office action under 35 USC 103(a), Applicants arguments and amendment are fully considered and the rejection is withdrawn herein in view of the amendment (cancellation of claims under the rejection).

9. The following are the rejections made in the previous office action under 35 USC 101 and 112, first paragraph (enablement):

Claims 3-7, 10, and 51 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

The claimed nucleic acids, vectors, host cells, and methods of making and using the nucleic acids are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid. The specification states that the FLEXGEM polynucleotides are useful in the diagnosis, prevention, and treatment of developmental, cell proliferative, and immunological disorders. The specification also teaches DNA sequences which encode FLEXGEM derivatives, or fragments useful in identifying or screening nucleic acid compounds encoding FLEXGE markers, to purify ligands and use as probe

arrays for gene expression. These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acid being claimed. Further, none of the recited utilities in the specification are specific to the SEQ ID No. 26. None rely on any unique feature of this nucleic acid, SEQ ID NO. 26.

Further, the claimed nucleic acids, vectors, host cells, and methods of making and using the nucleic acids are not supported by a substantial utility because while the specification teaches FLEXGEM encoding polynucleotides could be used in diagnosis, prevention, and treatment of developmental, cell proliferative, and immunological disorders, such diseases comprise a laundry

developmental, cell proliferative, and immunological disorders, such diseases comprise a laundry of diseases and disorders which do not make apparent "real world" use for the claimed polynucleotide. No substantial utility has been established for the claimed subject matter for example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acids have specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, or the laundry list of diseases they could be used to diagnose, prevent, or treat, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

The specification at table 4 teaches that the library from which SEQ ID No. 26 comes- was constructed using RNA from diseased breast tissue. However it does not establish that SEQ ID No. 26 is a marker for breast diseases or even any specific breast disease because the specification also teaches at table 3- that the SEQ ID No. 26 is expressed in various other reproductive, gastrointestinal and nervous tissue. The specification has not established any correlation between the expression of SEQ ID No. 26 and any specific disease or condition. Further experimentation would be required of the skilled artisan to reasonably confirm a real world use for the claimed polynucleotide and polypeptide it encodes.

As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claims 3-7, 10, and 51 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, the claims are not enabled for making or using a nucleic acid encoding fragment of SEQ ID NO: 26 (with regard to at least 90% identity). The specification does not teach the function or biological activity of SEQ ID NO: 6 or any specific amino acid fragments of SEQ ID NO: 6 that would provide the activity. Without a teaching of the biological function or activity of SEQ ID NO: 6 or a teaching of where and how to modify the polypeptide to produce a protein with the same or different functionality, the skilled artisan would be unable to

predictably determine what constituted a biological activity of a fragment of SEQ ID NO: 6, without extensive unpredictable trial and error analysis. While the specification teaches at table 2 that SEQ ID NO: 6 contains potential phosphorylation and glycosylation sites, such recitation does not make clear the specific biological function or activity of SEQ ID NO: 6. Further, the specification does not teach any specific assay to measure the biological activity of SEQ ID NO: 6. While the specification teaches the amino acid sequence of the polypeptide of SEQ ID NO: 6, one sequence does not enable a genus of biologically active polypeptide molecules based on the single structure disclosed in the instant application. Therefore, the ordinary artisan would be required to perform undue experimentation to identify any polypeptide, which was an active fragment of the polynucleotide of the presently claimed invention. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for its activity. Such experimentation would be replete with unpredictable trial and error analysis and is considered undue.

Response to Arguments:

With reference to the above rejection under 35 USC 101, Applicants arguments are fully considered and found not persuasive. On page 9-10 of the response, Applicants assert that the declarations and the ten scientific references submitted in parent case established the utilities of polynucleotides derived from nucleic acids expressed in one or more tissues / or cell types as hybridization probes, expression analysis in drug discovery, in toxicology, microarray expression profile and detection of a transcript expression. The assertions and arguments regarding the declarations and references submitted in the parent application are fully considered and found

not operable because declarations and evidence of support are not filed in the instant application. However, the asserted utilities and arguments are found not persuasive in the context of the claimed SEQ ID No. 26, because the disclosed utilities are non-specific utilities in the context of SEQ ID NO. 26, that is, the general utilities of a polynucleotide are not specific for the claimed SEQ ID No. 26, for which no specific function and activity is assigned. As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use – testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Thus general utility as a probe in hybridization, or a gene expression marker, does not constitute a specific utility for the claimed SEQ ID No.26. Thus the rejection is maintained herein.

With reference to the above rejection made in the previous office actions under 35 USC 112, first paragraph under enablement, Applicants' amendment and arguments are fully considered and found not persuasive. Applicants' argue that the claims have been amended to delete the fragment and the rejections be withdrawn these arguments are fully considered and found not persuasive because the current claims comprise the variant fragments with 90 % homology language, which comprises at least hundereds of thousands of fragments with unknown activity and which would require undue experimentation. Thus the rejection is maintained herein.

8. The following is the rejection made in the previous office action under 35 USC 112, first paragraph (written description):

Claims 3, 10, 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3, 10, 51are drawn to an isolated polynucleotide, fragments comprising of nucleotides of said polynucleotide having at least 90% identity to the SEQ ID NO. 26.

The specification teaches isolated polynucleotides referred collectively as "full length expressed genetic markers". The specification teaches isolated polynucleotide comprising SEQ ID NO. 26, expression of said polynucleotide in a host cell, and a vector carrying said polynucleotide. However, the breadth of the claims encompass a large genus of homologs of SEQ ID NO. 26, from any source, that have not been taught or described by the specification.

The claims are broadly drawn to nucleic acids sequences having at least 90% identity to the nucleotide sequence according to SEQ ID NO.26 and sequence complementary polynucleotides of said SEQ ID No. 26. Such recitation encompasses an extremely large genus of homologs of SEQ ID NO. 26, from any source. The recitation of polynucleotide having at least 90% identity with SEQ ID NO. 26, constitute an extremely large genus, wherein the disclosure of the single sequence of SEQ ID NO.26 is not representative of this large genus. Applicant has expressed possession of only one species in a genus, which comprises hundreds of millions of different sequences. The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or

features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common elements or attributes of the sequences are disclosed. The function of the encoded polypeptide is not disclosed, nor does the specification teach what constitutes a homolog fragment. The specification does not teach or describe which amino acids are critical for any function of the protein sequence of SEQ ID NO. 6. With regard to the fragment or a complementary sequence of SEQ ID No.26, the recitation of the single sequence of SEQ ID No. 26 is insufficient to demonstrate identity of biological activity or function in all of these different species where no structural information regarding where in the sequence the biological activity resides. With regard to a polynucleotide comprising at least 90% sequence identity- such recitation encompasses sequences with the same biological activity as well as sequences with different biological activity of SEQ ID No. 26. However, without a teaching of residues critical for any "biological activity' the skilled artisan would be unable to envision the structure of the encompassed homologs or fragments encoded by SEQ ID NO. 26.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO.26, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the

complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Response to arguments:

With reference to the above rejection under 35 USC 112, first paragraph, written description, Applicants arguments and amendment are fully considered and found not persuasive. Applicants argue that the claims are amended to delete the fragment language and regarding the "variant", having at least 90% homology to SEQ ID NO. 26, Applicants argue that

the instant specification discloses the encoded polypeptide with chemical structure as disclosed in the SEQ ID No. 6. Applicants' arguments are fully considered and found not persuasive because according to the written description guidelines, the specification should provide evidence that the applicant was in possession of the claimed invention i.e. "a complete or partial structure, other physical and / or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics". Applicants have claimed 90% partial structure with no coupled function. Applicants further argue that there is no requirement that the claims recite a particular amino acid variant, because the recited variants are defined in terms of SEQ ID No.6. Applicants' arguments are fully considered and found not persuasive because it is well known in the art that a single amino acid change in a protein would result in abolishing the function of said protein, (for example it is well known in the art that a single amino acid change in β- globin chain is responsible for sickle cell anemia due to aberrant protein function). As discussed above, a variant having 90% homology to SEQ ID NO. 26, comprise a large number of variants and variant proteins and the instant specification disclosed only one member of this large genus, SEQ ID No.6. Thus Applicants have shown possession of only one member, for which no information is disclosed regarding where in that member the biological function or activity is resided. This single member is not a representative of the genus of encompassed mutants, variants and homologs of SEQ ID No. 6.

On page 13 of the response, Applicants argue that one of ordinary skill in the art would recognize polynucleotide sequences which are variants having a polynucleotide sequence at least 90% identical to SEQ ID No. 26 and asserts that the specification provides adequate written

description of the recited polynucleotide variants of SEQ ID NO. 26. These arguments are fully considered and found not persuasive because the specification does not provide any guidance as to a correlation between the structure of these possible variants and their function.

Applicants further argue that the instant DNA claims are defined on the basis of structural features and are in accordance to the guidelines of written description. Applicants' arguments on the cited case law : Fiers v. Revel and Univ of California v. Eli Lilly and Co., are fully considered, but found not persuasive. In the instant case, the claims recite partial structure, and the genus of nucleic acids encompassed includes variants, mutants, and homologs from any source. The written description guidelines clearly indicate that a written description includes for example " functional characteristics when coupled with a known or disclosed correlation between function and structure...." . In the instant case, not only a correlation between structure (i.e., nucleic acids with at least 90% identity) and function is lacking (not provided), but the function of the full length sequence is also lacking from the specification – as such, it is not clear from the teachings in the specification as to what structural features of SEQ ID No. 6, provide a description of mutants with altered activity, or variants or homologs with the same or similar activity. Accordingly, the specification does not provide an adequate written description of the variants, mutants and homologs from any source, which are encompassed by the broadly claimed invention.

On page 17 of the response, Applicants assert that Brenner et al. teach sequence comparison analysis of a data set of proteins with known structural and functional relation and with < 90% overall sequence identity, Brenner et al. have determined 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least

150 residues and >= 40% identity over at least 70 residues is reliable in signifying homology between proteins. These assertions are fully considered, but found not persuasive. Although amino acid homology can identify proteins which belong in a certain class, such homology analysis is not sufficient to necessarily establish critical amino acids or domains, which are required for function. Additionally, Brenner provides an analysis regarding the relationship between proteins, wherein the structure and function of one of the proteins in the comparison is already known. In the instant claims, the function of SEQ ID No. 6 is not known; therefore it is unclear how the specification provides a description of the structure of a variant with altered activity, or the structure of a variant with the same or similar function. Two proteins can have a single amino acid different and all others in common and a single amino acid change can abolish the function of a protein. Therefore the structural identity alone does not provide any basis for its functional activity unless until a correlation between the structure and function (such as critical amino acids or domain) is established.

Applicants' arguments regarding the state of art (recombinant technology) at the time of the present invention and at the time of the Lilly and Fiers application, are fully considered. The assertion that one skill in the art would recognize that the present inventors are in possession of the broadly claimed invention, based on the sequence information of SEQ ID No. 6 and SEQ ID No. 26 and available recombinant technology, is fully considered and found not persuasive. The advancement in recombinant technology as pointed out by the applicants only provide the methodology that would be needed to determine the function of SEQ ID No. 6 and then determining the structure of a variant with altered activity or a variant with the same activity.

However, this is not a description of the actual sequences encompassed by the broad claims, but a discussion of how to go. Thus the rejection is maintained herein.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
August 13, 2004

Jehanne Sitton
JEHANNE SITTON
PRIMARY EXAMINER
8/13/04